A MEDICAMENT AND A METHOD OF TREATING ERECTILE DYSFUNCTIONS

Field of the invention

The preset invention relates to the field of medicine and can be used for treating the disturbances in erection of various origin and vegetative impairments during male climax.

Background of the invention

It is a well-known practice of the treatment of pathologic syndromes by the use of antibodies (SU 1331508 A, A 61 K 39/00, 1984; SU 1730144 A1, C 12 N 7/00, 1992).

The disturbances in erection can be treated by regulation of the levels of cyclic guanosine monophosphate (cGMP) in the cavernous bodies on sexual stimulation (see Register of Pharmaceuticals in Russia, Encyclopedia of Pharmaceuticals (in Russian), Moscow, 2001, pp. 788-789). This approach enhances the relaxing effect of nitric oxide (NO) on the smooth muscles of the cavernous bodies and increases penile blood flow through the administration of a direct inhibitor of cGMP-specific phosphodiesterase Type 5. However, the duration of this effect is limited to 3-5 hours and the agent used (sildenafil citrate) is contraindicated to persons receiving nitric oxide donors or nitrates in any form.

Description of the invention

The present invention is directed at obtaining an efficient medication for and a method of the treatment of erectile dysfunctions of various origin and of vegetative disorders of male climax.

The formulated objective is attained by using a medication containing an activated form of ultra-low doses of monoclonal, polyclonal or natural antibodies to endothelial nitric oxide synthase (NO synthase), the activated form being prepared by multiple consecutive dilutions and by exposure to external factors, preferably in accordance with homeopathic technology.

For preparing the antibodies one can use the entire molecule or polypeptide fragments of the enzyme (endothelial NO synthase).

The method of the treating erectile dysfunctions of various origin and of vegetative disorders of male climax through regulation of the level of cyclic guanosine monophosphate (cGMP) in the cavernous bodies on sexual stimulation involves the use of activated forms of ultra-low doses of antibodies to the entire molecule of endothelial NO synthase or to its polypeptide fragments, the activated forms being prepared by multiple consecutive dilutions and exposure to external factors.

Preferably, a mixture of various, mostly centemal, homeopathic dilutions of the antibodies indicated above should be employed.

The medication obtained in accordance with the present invention is a new pharmaceutical, which modifies the activity of NO synthase, thus intensifying the synthesis of nitric oxide in the cavernous bodies on sexual stimulation and enhancing the penile blood flow.

Unlike physiologic (therapeutic) doses of the antibodies, the activated forms of ultra-low doses of the antibodies to NO synthase do not bind (inactivate) the enzyme; instead, they modify its effects. The new medication has an effect synergic with that of NO synthase. The existence of the therapeutic effect of ultra-low doses of antibodies activated by homeopathic technology, as well as the unidirectional character of the action with the original enzyme do not follow from the state-of-the-art knowledge and have been discovered by the inventor.

Embodiments of the invention

The new pharmaceutical is preferably prepared in the following manner.

A synthetic polypeptide corresponding to the fragment of the endothelial (Type III) NO synthase (1185-1295) with the following amino acid sequence: Glu Arg Leu His Asp Ile Glu Ser Lys Gly Leu Gln Pro Thr Pro Met Thr Leu Val Phe is obtained by solid-phase peptide synthesis (Marsden PA, Schappert KT, Chen HS, Flowers M, Sundell CL, Wilcox JN, Lamas S, Michel T. Molecular Cloning and Characterization of Human Endothelial Nitric Oxide Synthase, FEBS Lett., 307:287-293, 1992).

The produced peptide, conjugated with methylated bovine serum albumin as a carrier, is used as an immunogen for immunization of rabbits. The monospecific serum to NO synthase is obtained by immunization of rabbits by this immunogen in accordance with a well-known procedure (Vyazov O.L. Laboratory Methods of Studies in Non-Infection Immunology (in Russian), Moscow, Meditsina, 1968, 356 pages). The blood is taken from an external ear vein into sterile test tubes. After the clot retraction, the serum is separated by centrifugation and heated at 56 °C for 10 min for complement inactivation.

The isolated antibodies to the endothelial NO synthase are subjected to consecutive multiple dilutions and exposed to an external mechanical impact until ultra-low or low doses are obtained, for example, according to homeopathic technology of potentization (see W. Schwabe, "Homöopathisches Arzneibuch", Stuttgart, 1978). This procedure gives rise to a uniform decrease in concentration through consecutive dilutions of 1 volumetric part of the initial matter (antibodies) in 9 volumetric parts (for decimal dilution, D) or in 99 volumetric parts (for centimal dilution, C) of a neutral solvent with multiple vertical shaking of each solution; the advantages of various containers for each subsequent dilution are used. Finally, this procedure gives the required dose (potency).

The external treatment in the course of concentration reduction can be also executed by exposure to ultrasonic, electromagnetic, or other physical factors.

The resultant medicines are used mostly in the dosage forms and dilutions adopted in the homeopathic practice: as alcoholic and aqueous solutions or as tablets (granules) prepared by impregnating the carrier contained in the dosage form by the potentised solution to saturation; also, the potentised solution can be added directly to a liquid dosage form.

Example 1

In studies of the effect of activated forms of ultra-low doses of antibodies to the endothelial NO synthase on the sexual behavior of adult male rats being under conditions of physiologic suppression of the reproductive function, we administered *per os* potentiated antibodies to NO synthase in a mixture of homeopathic dilutions C12 + C30 + C200 (within a period of 5 days, 1.5 ml per animal) to male rats 16 months old weighing 600-700 g with an established degree of sexual function suppression. After that, the male rats were placed with female rats (4 months old, weight 300 g) being in the estrous stage of the sexual cycle. Within 15 min we were registering the copulative activity on the basis of the following parameters for each male: latency of mounting (the period between the first presentation of the female and the first mounting), the number of courtships (sniffings, lickings), the total number of mountings, the number of copulations.

It was found that after 5 administrations of the preparation the number of courtships increased with high degree of significance (2 times) as against the initial indices of all animals; in 55.5 % of the animals (with the initial medium and pronounced sexual activity) the indices of sexual activity increased with high degree of significance. All this testified to the stimulating effect on the sexual activity of male rats present under the conditions of physiologic suppression of the reproductive function.

Example 2

In studies of the effect of activated forms of ultra-low doses of antibodies to endothelial NO synthase on the sexual behavior of adult male rats being under conditions of seasonal suppression of the reproductive function we administered *per os* potentiated polyclonal antibodies to NO synthase in a mixture of homeopathic dilutions C12 + C30 + C200 (within a period of 5 days, 1.5 ml per animal) to male rats 4 months old weighing 400-450 g. After that, the male rats were placed with female rats (4 months old, weight 300 g) being in the estrous stage of the sexual cycle. Within 15 min we were registering the copulative activity on the basis of the following parameters for each male: the latency of mounting (the period between the first presentation of the female and the first mounting), the number of courtships (sniffings, lickings), the total number of mountings, the number of copulations.

It was found that after 5 administrations of the preparation the latency of mounting in the test group decreased with high degree of significance; at the same time, we observed an increase in the total number of mountings (2-fold) and in the number of copulations (3-fold) as against the indices obtained for the animals before administration of the drug. Thus, the administration of the preparation gave rise to the improvement of the copulative activity in male rats being under the conditions of seasonal suppression of the reproductive function, the improvement being manifested in the animals' need for repeated coitions. The accompanying decrease in the number of courtships was caused by a higher copulative activity.

Example 3

Patient S. (male), aged 51, applied to the urologist with a complaint about decreased libido, erection impairment, and lowered satisfaction from the coitus. These symptoms had been aggravating during previous two years. Over the recent 3 years the patient had been marking periodic suppressed mood, whining, memory and sleep disorders, lowered

working capacity, palpitation fits, instability of the arterial blood pressure. Clinical findings: a moderate enlargement of the prostate gland. Diagnosis: erectile dysfunction against the background of involutional hormonal changes. Prescription: a mixture of homeopathic dilutions C12 + C30 + C200 of monoclonal antibodies to a fragment of human endothelial NO synthase, 1 tablet every 3 days. Two weeks after the beginning of treatment the patient noted better erection and an enhancement of libido against the background of the improvement of the general condition: the overall tonicity rose and the sleep became better. The recommendation was to take the preparation 1-2 times a week. On the second visit 2 months after the beginning of the treatment the patient presented no complaints; he regained libido, erection, and satisfaction from the coitus.